THE THEOLOGY OF BIOLOGICAL WARFARE

Paul Kraemer

Our cartoon of a microbiology laboratory reflects the ultimate in nonchalance. Of course, the punch lines of the two scientists might apply equally well in a nuclear bomb facility. For instance, when J. Robert Oppenheimer witnessed the first nuclear explosion at Trinity site in July 1945, it is reported that he compared it to a demonstration of the power of Vishnu. This is the Hindu god who transformed himself into the "Destroyer of Worlds" in chapter 11 of the Bhagavad Gita. Oppenheimer was evidently quite taken with the ancient Hindu scriptures. He could read the Gita in the original Sanskrit and discuss the religious issues at length. According to his friend Charles Critchfield, he also loved to make dramatic or startling statements, a tendency that was to get him into trouble later. At any rate, in this Gita version of the Hindu religion, God does everything, good and evil, creates and destroys, with no Devil or Satan needed. Periodically, when God so elects, he destroys most of mankind and then has room to create new people, sort of like selecting "erase disk and restart" on your computer.

Regardless of what Oppenheimer really believed, since 1945 the possibility of a nuclear holocaust has been thoroughly examined using theological models in the Judeo-Christian tradition. This tradition is rich in apocalyptic and millennial prophesies and generally invokes a force of evil separate from God: Satan, the Devil, the Antichrist, or the

Paul Kraemer is an emeritus scientist with the Biological Sciences Division of Los Alamos National Laboratory. He has authored more than ninety papers on microbiology and related fields (E-mail: kraemer@telomere.lanl.gov).

"Beast." The end of the world, including dangers due to nuclear weapons, has been a theme of theologians ranging from serious academic scholars to the lunatic fringe. The popularity of the subject is suggested by finding that the Barnes and Noble bookstore currently lists 1,588 titles under the key word *eschatology* (end-of-the-world theology) on its Web site.

Worldwide, nuclear matters have evidently caused theologians, politicians, and nearly everybody else to overlook the increasing danger of biological warfare. Unfortunately there are good reasons to suggest that a general disaster of apocalyptic magnitude will more likely be biological in nature. The prevention of and defense against biological warfare are more difficult than the nuclear problem. Biological agents have been used in warfare for centuries, but nobody has ever won a war using natural pathogens such as anthrax or smallpox. Today, however, the technology is in place and publicly available to create genetically engineered pathogens that are capable of massive destruction of humanity. The problems posed by this threat are inherently more difficult than those associated with nuclear warfare.

Leaving aside theological aspects for the moment, a direct cause of this new danger is recent rapid technological developments, particularly in genomics (information derived directly or indirectly from genetic sequence data). This field is moving so fast and yielding so many biological insights daily that it is difficult for even scientists working in the field to fully comprehend its potential. However, our cartoon, which portrays a microbiology laboratory in the imminent future, includes facilities for using genomics relevant to biological warfare research.

The incubator labeled "genetically enhanced pathogens" contains the products of that research. Are not natural pathogens like anthrax and plague bad enough? That depends. Bad enough for a terrorist who wants to kill a few hundred or even a few thousand people. In fact, the Army (Medical Research Institute of Infectious Diseases) and the National Institutes of Health, at least publicly, have trivialized the larger problem by focusing only on this aspect. It is certainly true, for instance, that a handful of smallpox cases in New York City would cause a problem. All available smallpox vaccine would be used up quickly, since none has been made since 1980. The World Health Organization prematurely declared that smallpox had been eradicated in 1977 and discontinued vaccination programs in 1980. Vaccine production was quickly dismantled. But in the year 2000, we learned that the Soviet Union had been making huge stockpiles of "weaponized" smallpox virus, the fate of which is still unclear. (The Soviet Union, in massive violation of its treaty commitments, had sixty thousand people, at thirty-six scattered installations, secretly working on biological weapons.) Since 1980, susceptibility to smallpox has risen to about 83 percent of the world's human population.

NATURAL EPIDEMICS

It is historically true that natural pathogens have occasionally caused epidemics of sufficient magnitude to be nearly apocalyptic. Sixteenth-century Mexico lost 90 percent of its native population due to successive waves of smallpox and measles. In the middle of the fourteenth century, plague (the Black Death) wandered all over Asia, the Middle East, North Africa and Europe for seven years, killing 20 to 50 percent of the

Today, the technology is in place and publicly available to create genetically engineered pathogens that are capable of massive destruction of humanity.

population wherever it passed.

Nevertheless, natural pathogens, even at their worst, are not optimized for the purposes of full-scale biological warfare. Speed is important to surprise both the individual human body under attack and the society of which the individual is a member. It takes time for the host to mount its defenses, and it takes time for society to respond. Genetic modifications of viruses, by techniques now available to anyone, can make these contests very different than they are in nature. Let me give one example of the hundreds that can be hypothesized.

Influenza virus has a very short incubation period and is one of the most contagious natural pathogens known. Once in a while a "pandemic" strain emerges in nature from a rare recombination of a human strain with an animal or bird strain. Nobody has any residual immunity to these totally new creatures, which can quickly sweep across the planet. The worst strain so far was the Spanish flu of 1918–19, which infected almost everybody in the world and killed over twenty million people. But it was not apocalyptic—the mortality rate was about 0.5 percent—and it did not destabilize any nations or society in general.

The low death rate is primarily due to the fact that the influenza infection is almost completely restricted to the respiratory tract, unlike its relative, the measles virus, where the primarily infected respiratory cells always release virus into the bloodstream. Research has shown that a protein of the influenza virus, called M2, is involved in directing the newly formed virus to the outside surface of the cells lining the respiratory tract (called "apical" release), in contrast to release at the "basal" surface toward the blood vessels. Sounds complicated, which it is, but how would you like it if Osama bin Laden, the terrorist leader, sent a dozen of his suicide agents hacking and coughing on a seven-day odyssey through the international airports of the world, after being infected with a created pandemic strain of influenza virus that contained an engineered M2 gene? Just hanging around London-Heathrow airport, which is usually packed with people from everywhere going everywhere, might do it. There is even a well-established cell-culture model that can be used for the preliminary work on apical/basal shedding of influenza virus.

NEW TECHNOLOGIES OF DISEASE-GENE CREATION

The current technical ability to create hundreds of innovative viruses of unprecedented virulence is a consequence of the new genomics technologies. The basic idea of genomics is straightforward: The sequence of the entire genetic apparatus of an organism is determined, and then, using this database, the functions of each and every portion of that apparatus (genome) are gradually worked out using a wondrous array of new techniques. Sequence databases have recently been completed for humans as well as for several other creatures and many important pathogens. Working out the functional genomics for humans is still

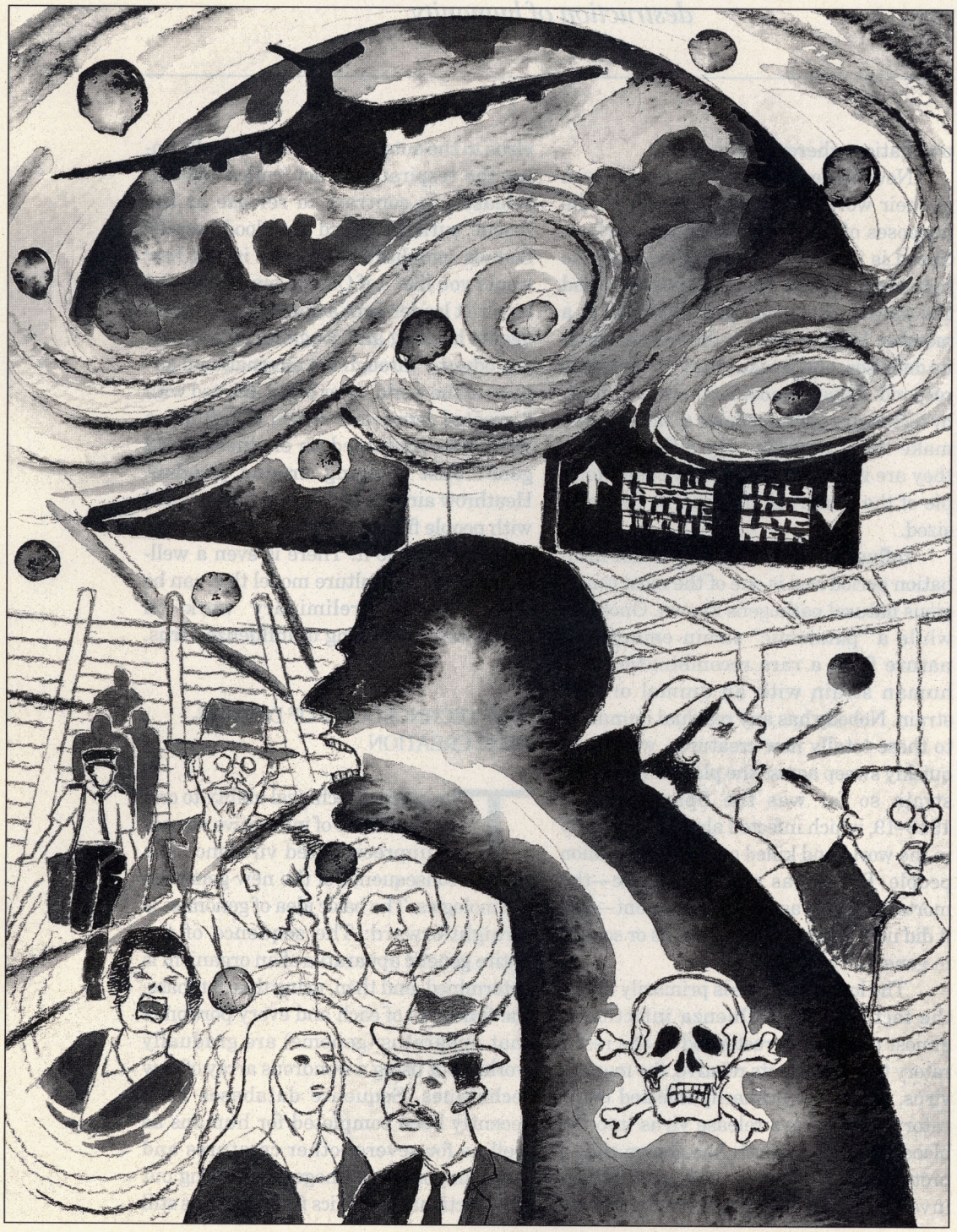

ILLUSTRATION BY MARCIA KLOZE HUGHES / THE WORLD & I

The era of designer genes and cut-and-paste viruses has already arrived.

in its infancy because people's genomes are very large, containing almost 100,000 genes as well as a lot of regulatory and structural stuff. Viruses typically have genomes at least three orders of magnitude smaller, with at most about 200 genes (influenza virus has about a dozen genes). Mountains of functional data about viruses are now pouring out of research laboratories all over the world. All these databases and functional results are freely available to the public.

Our cartoon shows one of the scientists using a microbial sequence database called a "Superannotated Diabolical Database." This is pure fiction—right now. At least I don't know of any public databases so named; private ones that are equivalent are undoubtedly in progress. Annotation refers to the references and other data that are tagged to sequence segments and represent the accumulating functionally relevant data. In the case of a "Diabolical Database," the sequence segments of pathogenic microorganisms are tied to functions relevant to biological warfare: incubation period, infectivity, shedding characteristics, cell culture models, all possible virulence parameters, and stability in aerosols. In other words, the database contains not just clinical virology data but the genetic determinants of those characteristics that make for enhanced pathogenicity. The era of designer genes and cut-and-paste viruses has already arrived.

The signs on the cartoon laboratory door are largely macabre, insider exaggerations, but they illustrate several points. There is no official meaning to BSL 6 1/2. Biosafety Level 4 is currently the highest level of laboratory precautions and is used for many operations involving the most dangerous viruses, such as in Ebola virus research. Our BSL 6 1/2 is meant to suggest that this might be a suitable designation for a laboratory where the final engineered viruses are grown before being submitted to rapid serial passage in human prisoners kept in a BSL 7 facility. This is also to remind the reader that there really have been some monstrous evils in this biological warfare business. Between 1937 and 1945, the infamous General Ishii of the Japanese army, at a complex in Manchuria called Unit 731, used thousands of Chinese nationals to develop weaponized anthrax aerosols. Almost three thousand deaths were documented after the war.

In contradiction of the BSL 6 1/2 designation is the sign "Biothreat Reduction Laboratory" denoting a defensive laboratory. Therein lies a problem that seems to lack any easy solution. How can one distinguish a laboratory that is designing biological warfare agents from one that is investigating defensive strategies, or, for that matter, *any* infectious disease research laboratory? They all look alike and use the same public databases, technology, and materials, as well as personnel with similar skills. There are thousands of legitimate microbiology laboratories all over the world, including institutes, pharmaceutical companies, academic departments, and government laboratories, doing beneficial infectious disease research. Their work includes developing vaccines, devising new methods of therapy, and trying to understand

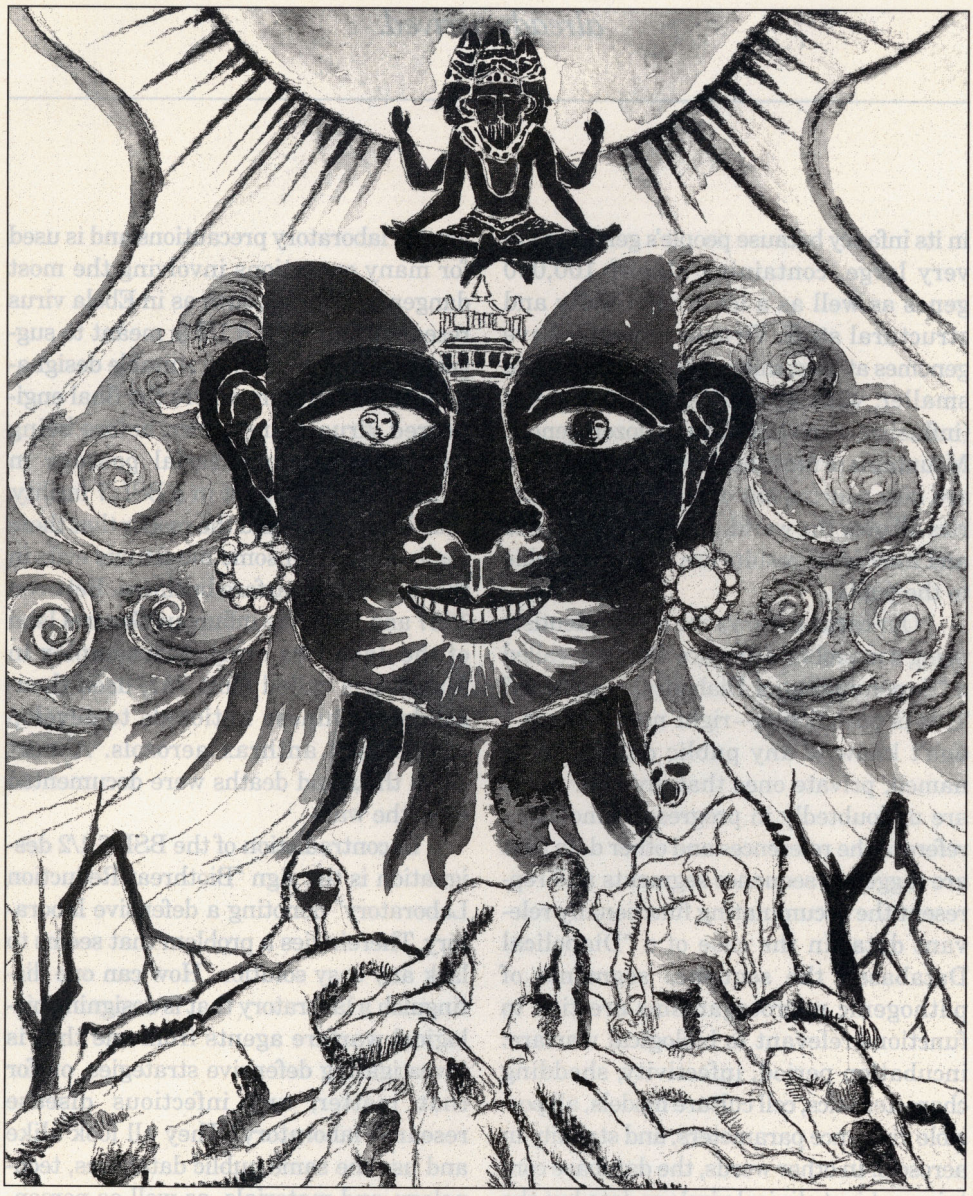

ILLUSTRATION BY MARCIA KLIOZE HUGHES / THE WORLD & I

disease mechanisms. Any of these places could be a cover for creating genetically enhanced pathogens. Such activities could even be pursued without the knowledge of their own management.

Unlike nuclear weapons facilities, biological warfare research doesn't require large national organizations or billions of dollars. An organization of a half dozen skillful people with a few million dollars could locate almost anywhere and stand the world on its head. Conspicuous equipment such as large fermenters is not needed. As the technology becomes easier to use and more accessible, the number of people who will want to play this apocalyptic game will increase substantially. At the same time, the rate of development of

Today many experienced microbiologists shy away from any involvement with even defensive programs in this area.

defensive strategies, which are intrinsically more difficult to implement, will lag further behind. As one sarcastic observer wrote, it won't help having a bunch of FBI people in space suits running around after a large part of a population has been exposed to an untreatable, optimized bioagent.

THEOLOGY AND WORLDVIEWS

Well, what has theology got to do with all this? It has to do with what kind of worldviews our society can sustain in a world that seems to be accelerating toward some kind of climax. Of course, we could avoid thinking about it or "have faith." Many people, including many scientists, believe that the word *nature* is roughly equivalent to the word *God*, except that the former is scrubbed fairly clean of speculative theology and anthropomorphic similes. In the small world of experimental biology from which I come, nature is rarely worshiped; a more common reaction after a particularly frustrating experiment is the expression, "Nature is a b——." I don't know where the gender designation came from. And hardly anybody in or out of science thinks of nature as necessarily kind. Generally speaking, however, there is never any question about who is boss, and that makes nature equivalent to God in a nonspeculative theology.

Erasmus tried to warn the Catholic Church about the dangers of codifying speculative theology five hundred years ago. The church couldn't decide whether to make him a cardinal or burn him at the stake (this is my interpretation of history; other interpretations are abundant). So here we are starting the third millennium C.E., and it seems clear that our most brilliant achievements have very serious unintended consequences. This appears to be the case with microbial genomics. Besides, there are way too many people now. Seems like a good time for an apocalypse. Or, to express the hypothesis less flippantly, a global, decimating biological catastrophe would be a natural event akin to the mass suicide of lemmings.

I don't necessarily believe all of that last paragraph, but I think it is worth a thought. A more common reaction when people learn something about biological warfare is "Scary, I don't want to think about it." The United States dismantled its biological weapons programs in 1969. Still, today many experienced microbiologists shy away from any involvement with even defensive programs in this area. A fairly sterile position has been taken nationally by the powers that be. That is, be vigilant and put your trust in international treaties. Such treaties have already proved pathetically unenforceable and will be even more irrelevant in the future as the players become less well defined and more numerous. If anybody has better ideas than these, now is the time to start pushing them forward.

On a positive note (and this is the best I can come up with for a final positive note), unlike those who survived a nuclear holocaust, the survivors of biological warfare would inherit a beautiful world with human infrastructure largely intact.■